PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 08 August 2000 (08.08.00)	
International application No. PCT/US99/28793	**Applicant's or agent's file reference** 03063-0561WP
International filing date (day/month/year) 07 December 1999 (07.12.99)	**Priority date** (day/month/year) 07 December 1998 (07.12.98)
Applicant TSANG, Victor, C., W. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

07 July 2000 (07.07.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Antonia Muller
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
A61K 39/395, G01N 33/569, 33/577, A61P 33/00 // C07K 16/20

A1

(11) International Publication Number: WO 00/33873

(43) International Publication Date: 15 June 2000 (15.06.00)

(21) International Application Number: PCT/US99/28793

(22) International Filing Date: 7 December 1999 (07.12.99)

(30) Priority Data:
60/111,225 7 December 1998 (07.12.98) US

(71) Applicant *(for all designated States except US)*: THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY, HEALTH AND HUMAN SERVICES [US/US]; Center for Disease Control and Prevention, Office of Technology Transfer, Executive Park, Building 4, Suite 1103, Atlanta, GA 30329 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: TSANG, Victor, C., W. [US/US]; 2595 Oak Crossing Drive, Decatur, GA 30033 (US). CALL, Jeffrey, L. [US/US]; 2471 LeHaven Drive, Tucker, GA 30084 (US). LEE, Yeuk-mui [US/US]; 4920 Winters Chapel Road, E-3, Doraville, GA 30360 (US). HANCOCK, Kathy [US/US]; 1488 N. Amanda Circle, Atlanta, GA 30329 (US).

(74) Agents: GREENE, Jamie, L. et al.; Jones & Askew, LLP, 2400 Monarch Tower, 3424 Peachtree Road, N.E., Atlanta, GA 30326 (US).

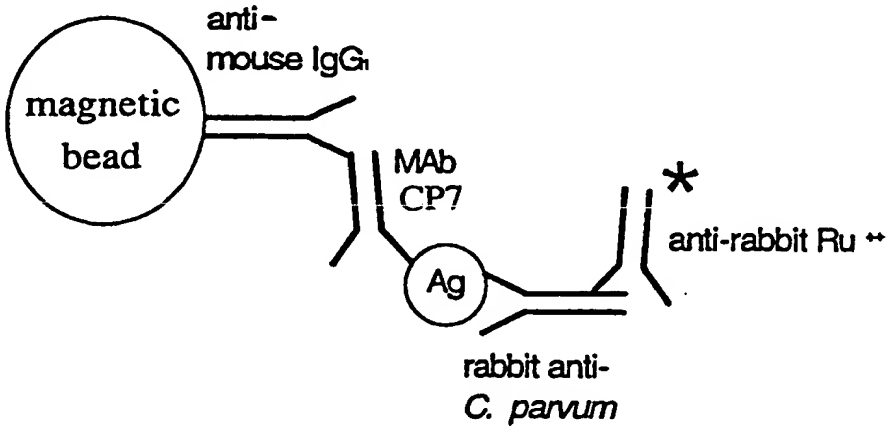
(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: REAGENT AND METHOD FOR DETECTING A CRYPTOSPORIDIUM PARVUM SPOROZOITE ANTIGEN

(57) Abstract

A reagent and method for the specific and highly sensitive detection of *C. parvum* in which the reagent is an antibody for a soluble *C. parvum* sporozoite antigen and the method is an immunoassay in which the antibody is used to detect or quantify *C. parvum* sporozoite antigen in a sample. The sample is treated to cause excystation of *C. parvum* oocysts, thereby releasing a *C. parvum* sporozoite antigen, and combined with antibodies specific for the sporozoite antigen under conditions to form an antibody–antigen complex. Detection of the complex indicates the presence of *C. parvum* in the sample. The assay allows recognition and detection of *C. parvum* in turbid samples, and due to a lack of crossreactivity with other *Cryptosporidium* species, is specific for *C. parvum* contamination or infection. The assay is highly sensitive, allowing for the detection of less than 100 oocysts per milliliter of sample.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
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AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
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BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
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CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
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DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

Int. tional Application No
PCT/US 99/28793

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/395 G01N33/569 G01N33/577 A61P33/00 //C07K16/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 07320 A (NORTH CAROLINA STATE UNIVERSITY) 26 February 1998 (1998-02-26) examples claims ---	1-4, 6-10,14, 15
X	WO 97 36612 A (M. RIGGS ET AL.) 9 October 1997 (1997-10-09) examples claims --- -/--	1-4, 6-10,14, 15

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 May 2000	23/05/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Nooij, F

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	M. RIGGS ET AL.: "Neutralization-sensitive epitopes are exposed on the surface of infectious Cryptosporidium parvum sporozoites." THE JOURNAL OF IMMUNOLOGY, vol. 143, no. 4, 15 August 1989 (1989-08-15), pages 1340-1345, XP002137132 Baltimore, MD, USA the whole document	1-4, 6-10,14, 15
X	M. RIGGS ET AL.: "Protective monoclonal antibody defines a circumsporozoite-like glycoprotein exoantigen of Cryptosporidium parvum sporozoites and merozoites." THE JOURNAL OF IMMUNOLOGY, vol. 158, no. 4, 15 February 1997 (1997-02-15), pages 1787-1795, XP002137133 Baltimore, MD, USA the whole document	1-4, 6-10,14, 15
X	F. ENRIQUEZ ET AL.: "Role of immunoglobulin A monoclonal antibodies against p23 in controlling murine Cryptosporidium parvum infection." INFECTION AND IMMUNITY, vol. 66, no. 9, September 1998 (1998-09), pages 4469-4473, XP002137134 Washington, DC, USA abstract	1-4, 6-10,14, 15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/28793

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9807320 A	26-02-1998	AU 4234597 A	06-03-1998
		EP 0961547 A	08-12-1999
WO 9736612 A	09-10-1997	AU 2721897 A	22-10-1997

PATENT COOPERATION TREATY

SCANNED

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
JONES & ASKEW, LLP
Attn. Greene, Jamie L
2400 Monarch Tower
3424 Peachtree Road, N.E.
Atlanta, GA 30326
UNITED STATES OF AMERICA

RECEIVED
MAY 31 2000
Jones & Askew

	Date of mailing (day/month/year) 23/05/2000
Applicant's or agent's file reference 03063-0561WP	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/US 99/28793	International filing date (day/month/year) 07/12/1999
Applicant THE GOVERNMENT OF THE UNITED STATES..ET AL	

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the International application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the International application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for International publication.

Within **19 months** from the priority date, a demand for International preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Nina Vercio

Form PCT/ISA/220 (July 1998)

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international pbulication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped),whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
03063-0561WP		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 99/ 28793	07/12/1999	07/12/1998
Applicant		
THE GOVERNMENT OF THE UNITED STATES..ET AL		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   REAGENT AND METHOD FOR DETECTING A CRYPTOSPORIDIUM PARVUM SPOROZOITE ANTIGEN

5. With regard to the **abstract**,

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

   [X] as suggested by the applicant.

   [ ] None of the figures.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International Application No
US 99/28793

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/395 G01N33/569 G01N33/577 A61P33/00 //C07K16/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 07320 A (NORTH CAROLINA STATE UNIVERSITY) 26 February 1998 (1998-02-26) examples claims ---	1-4, 6-10,14, 15
X	WO 97 36612 A (M. RIGGS ET AL.) 9 October 1997 (1997-10-09) examples claims --- -/--	1-4, 6-10,14, 15

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 May 2000	23/05/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Nooij, F

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	M. RIGGS ET AL.: "Neutralization-sensitive epitopes are exposed on the surface of infectious Cryptosporidium parvum sporozoites." THE JOURNAL OF IMMUNOLOGY, vol. 143, no. 4, 15 August 1989 (1989-08-15), pages 1340-1345, XP002137132 Baltimore, MD, USA the whole document	1-4, 6-10,14, 15
X	M. RIGGS ET AL.: "Protective monoclonal antibody defines a circumsporozoite-like glycoprotein exoantigen of Cryptosporidium parvum sporozoites and merozoites." THE JOURNAL OF IMMUNOLOGY, vol. 158, no. 4, 15 February 1997 (1997-02-15), pages 1787-1795, XP002137133 Baltimore, MD, USA the whole document	1-4, 6-10,14, 15
X	F. ENRIQUEZ ET AL.: "Role of immunoglobulin A monoclonal antibodies against p23 in controlling murine Cryptosporidium parvum infection." INFECTION AND IMMUNITY, vol. 66, no. 9, September 1998 (1998-09), pages 4469-4473, XP002137134 Washington, DC, USA abstract	1-4, 6-10,14, 15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/28793

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9807320 A	26-02-1998	AU 4234597 A	06-03-1998
		EP 0961547 A	08-12-1999
WO 9736612 A	09-10-1997	AU 2721897 A	22-10-1997

PATENT COOPERATION TREATY

NR

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JAN 0 8 2001

NEEDLE & ROSENBERG

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

GREENE, Jamie L.
JONES & ASKEW, LLP
2400 Monarch Tower
3424 Peachtree Road, N.E.
Atlanta, GA 30326
ETATS-UNIS D'AMERIQUE

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DEC 18 2000

14114.0358P1

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	13.12.2000
Applicant's or agent's file reference 03063-0561WP	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/28793	07/12/1999	07/12/1998

Applicant
THE GOVERNMENT OF THE UNITED STATES... et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

DEH/MLM/TMH
DOCKETED
By MW Date 1/8/01
Reviewed MLM 1/8/01
Name / Date

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Digiusto, M Tel.+49 89 2399-8162

Form PCT/IPEA/416 (July 1992)

09/857539

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
03063-0561WP		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/28793	07/12/1999	07/12/1998
International Patent Classification (IPC) or national classification and IPC A61K39/395		
Applicant THE GOVERNMENT OF THE UNITED STATES... et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07/07/2000	13.12.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Tilkorn, A-C Telephone No. +49 89 2399 8688

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/28793

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-35,37-39	as originally filed			
36	as received on	10/07/2000	with letter of	07/07/2000

Claims, No.:

1-16	as originally filed

Drawings, sheets:

1/6-3/6,5/6,6/6	as originally filed			
4/6	as received on	10/07/2000	with letter of	07/07/2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:
   ☐ the claims, Nos.:
   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 4.

because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

   ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

   ☒ the claims, or said claims Nos. 4 are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.
   ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;

citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	5-16
	No:	Claims	1-3
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-3, 5-16
Industrial applicability (IA)	Yes:	Claims	1-3, 5-16
	No:	Claims	-

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item III

Claim 4 does not satisfy Art 5 PCT for the following reason: The subject-matter of the claim is defined by a negative feature, namely by the fact that the antibody does not cross-react with other Cryptosporidium species. The prior art documents are silent about the cross-reactivity of the disclosed antibodies with other Cryptosporidium species.
Since neither the present invention nor the majority of the prior art documents precisely define the antigens to which the antibodies are directed, it appears an undue burden for the skilled person to determine the scope of the claim.
Thus, no opinion is given on novelty, inventive step and industrial applicability of claim 4 (Art 34 (4)(a)(ii) PCT).

Re Item V

The following documents are referred to in this communication:

D1: WO 98 07320 A (Feb 1998)
D2: WO 97 36612 A
D3: THE JOURNAL OF IMMUNOLOGY, vol. 143, no. 4, 15 August 1989, pages 1340-1345
D4: THE JOURNAL OF IMMUNOLOGY, vol. 158, no. 4, 15 February 1997, pages 1787-1795
D5: INFECTION AND IMMUNITY, vol. 66, no. 9, September 1998, pages 4469-4473

1 Novelty (Art 33(2) PCT):

1.1 **Claims 1** and **2** are anticipated by each of the documents D1-D5, since all the documents disclose antibodies specific for a soluble antigen of a C.parvum sporozoite (D1: p 14 l 1-6: mAb C6B6; D2: abstract: mAb 3E2; D3: p 1344 col 1 para 3: mAb 17.41; D4: abstract: mAb 3E2; D5: p 4471 col 2 para 2; Table 2: mAb G9H4).

1.2 D3 is detrimental to the novelty of **claim 3** (D3: p 1341 col 2 para 4: mAb which

bind to sporozoites only).

1.3 The specific deposited antibody is considered novel (**Claim 5**).

1.4 **Claims 6-16** are novel because none of the available documents discloses a method for the detection of C. parvum in a sample using an antibody specific for a soluble antigen of a C. parvum sporozoite.

2 Inventive Step (Art 33(3) PCT):

2.1 The subject-matter of **claim 5** does not appear to be inventive for the following reasons:
Each of the documents D1-D5 discloses one or more monoclonal antibodies directed to C. parvum sporozoite antigens (see V 1.1 above). The antibody CP7 with the accession number CRL-12604 appears to be functionally equivalent to the known antibodies. Inventive activity could only be acknowledged if the claimed antibody achieved an effect over the antibodies known in the art.

2.2 **Claim 6** does not appear to involve inventive activity for the following reasons:
As set forth in the description (p 6 l 33- p 7 l 6) the detection of C. parvum oocysts in clinical samples using monoclonal antibodies is known in the art.
The subject-matter of **claim 6** is distinguished from the prior art method in the antibody which according to the present claim is directed to a soluble sporozoite antigen whereas the prior art method apparently relies on an antibody specific for an oocyst antigen.
The problem to be solved can thus be regarded as the provision of a more sensitive and accurate detection method for C. parvum (appl.: p 7 l 1-6).
Antibodies directed to soluble sporozoites of C. parvum are well known in the art (see D1-D5). The same applies to excystation methods (D1: p 13 l 24-29, D3 p 1340 col 2 para 4; D5: p 4469 col 2 last line - p 4470 col 1 para 1). As the use of antibodies for the detection of analytes is commonplace in the art, the skilled would consider the detection of C.parvum in a sample using the known antibodies. Moreover, it seems obvious for the skilled person that detection methods involving antibodies directed to soluble antigens are more sensitive than detection methods involving antibodies directed to particles like oocysts. Consequently, the subject-

matter of **claim 6** appears to be obvious for the skilled person. Since the dependent **claims 7-16** do not contain an inventive concept per se, they do not seem to comply with Art 33(3) PCT either.

Re Item VII

- Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D5 are not mentioned in the description, nor are these documents identified therein.

- The expression "incorporated herein by reference" in respect of prior art documents (e.g. page 39 para 2) leads to a doubt as to whether the requirement of the description being self-contained is satisfied (Guidelines II, 4.17).

- The definition of the terms "a", "an" and "the" given in the description (p 12 18-20) deviates from the common meaning of the words and thereby renders the scope of the claims unclear. Thus, this paragraph should have been deleted from the description.

Re Item VIII

1 **Claims 3** and **4** do not satisfy Art 6 PCT because the expression "minimal cross reactivity" is a relative term which renders the scope of the claims unclear.

2 It is clear from the description on pages 7 l 30 - p 8 l 7 and p 13 l 9-10 that the following features are essential to the definition of the detection method according to the invention:

(1) using an antibody having binding specificity for a soluble C. parvum sporozoite antigen and exhibiting minimal or no cross reactivity with oocyst proteins or peptides
(2) treatment of the sample to excyst C. parvum oocysts

Since independent **claim 6** does not contain these features it does not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b)

PCT that any independent claim must contain all the technical features essential to the definition of the invention.

3 **Claim 15** does not comply with Art 6 PCT, because the expression "biological mechanism" is vague and renders the scope of the claim unclear. Moreover, there is no example for a "biological mechanism" in the description. The only example for the excystation for viability assays (appl.: p 29 l 33- p 30 l 12) involves incubation in an excystation buffer containing sodium taurocholate and vortexing. Hence, the claim lacks technical support in the description (Guidelines III 6.3).

Example 4
C. Parvum Immunoassay Specificity Analysis

Specificity of monoclonal antibody CP7

The specificity of the monoclonal antibody CP7 was determined by testing its ability to capture antigens from other closely related *Cryptosporidium* species and other protozoan parasites that may be encountered in environmental water samples. Aliquots containing 1 x 10^5 organisms of *C. parvum*, *C. baileyi*, *C. muris*, *C. serpenti*, *Giardia duodenalis*, *Eimeria papillate*, and *E. nieschulzi* were exposed to freeze/thaw cycles and assayed. The ECL signal from the freeze/thawed *C. parvum* oocysts was in excess fifty fold that of background. *Cryptosporidium parvum* was the only organism that produced a ECL signal above background as shown in Figure 4.

Example 5
C. Parvum Viability in Turbid Environmental Water Samples

C. *parvum* oocysts used for polyclonal and monoclonal antibody production were prepared and optimized according to the methods described in the Examples set forth above.

Environmental samples

To provide environmental water for evaluating the detection limits of the CP7 viability assay, Pall Gelman Envirochek™ filters (Pall Gelman, Ann Arbor, MI) were used to concentrate water samples from two sites. The first site was Kelly Cofer Lake, a 5.5 surface acre urban lake with an initial turbidity of 6.0 NTUs (Turbidimeter, Industrial Chemical Measurement, Hillsboro, OR). The second site was near a municipal water intake for DeKalb Co., GA, on the

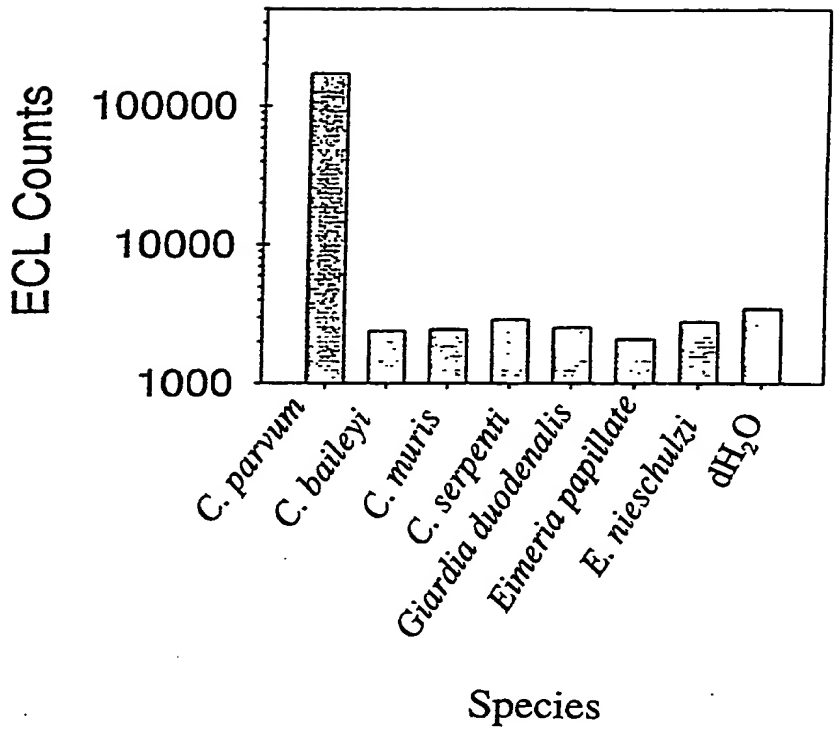
ECL Counts
100000
10000
1000
C. parvum
C. baileyi
C. muris
C. serpenti
Giardia duodenalis
Eimeria papillate
E. nieschulzi
dH2O
Species

Figure 4